

SPECIFICATION AMENDMENTS

Please replace the following amended paragraphs:

Page 5 , lines 18 to 26 insert the following paragraph:

According to a seventh aspect of the invention, there is provided a method of inhibiting hemangioma comprising administering to an individual in need of such treatment an effective amount of virally-administered small interference RNA (SiRNA) corresponding to a portion of CRT mRNA, wherein expression of the SiRNA decreases the level of CRT. The siRNA will be generated corresponding to the nucleotide 1917-1937 ~~4946-4936~~ of SEQ ID NO. 1, the DNA sequence in Figure 16 (sequences of sense 5'-GCU GAU CGU GCG GCC GGA CAA dTT 3', and anti-sense 5'- UUG UCC GGC CGC ACG AUC AGC dTT 3'). This siRNA has been shown to significantly diminish the expression of CRT (Troussard et.al., 2003).

Page 9, line 25 insert the following paragraph

Figure 17 – Nucleotide and amino acid sequence of SM22 α -CRT-HA (SEQ ID No. 12).

Page 10, lines 4 to 14, insert the following paragraph

As used herein, "calreticulin" or CRT, depending on the context, refers to a peptide encoding CRT as shown in Figure 16 or 17, a cDNA encoding CRT as shown in Figure 16 or 17, a cDNA molecule deduced from said peptide sequence, or a bioactive fragment or mutant or variant, either inter-species or intra-species, form thereof. As will be appreciated by one of skill in the art, a variant may be CRT from a different species which has at least 60% homology, or at least 70% homology or at least 80% homology to CRT amino acid sequence shown in Figure 16 (SEQ ID No. 23) or is a peptide known or believed to be related to or functionally homologous to CRT or a bioactive fragment thereof. As used herein,

"bioactive" with regard CRT indicates that the fragment or mutant form of CRT retains substantially normal or biological CRT activity.

In the paragraph bridging page 16, line 28 to page 17, line26, please insert the following paragraph:

SMCRT transgenic mice- A truncated SM22 α promoter (445 1343 base pairs of the 5' flanking region) which has been shown to target the Lac Z reporter gene expression in the vascular smooth muscle cells (specifically in the arterial side) but not other smooth muscle cells in the mouse embryo (Li et al., 1996) was used. We obtained this promoter from Dr. E. Olson (Southwestern Medical Centre, University of Texas, Dallas, USA) and cloned it upstream of mouse CRT cDNA tagged with HA epitope (HA-CRT). The epitope tag was used to differentiate between the expression of the transgene and the endogenous CRT. However, as will be appreciated by one of skill in the art, any suitable tag known in the art may be used if so desired. This plasmid was then used to generate a transgenic mouse overexpressing HA-CRT (SMCRT) in the vascular smooth muscle cells. The genotype of these mice was confirmed by PCR of the genomic DNA with primers specific to the sequence of SM22 α (5' primer) and CRT (3' primer). The expression of the HA-CRT in these mice was detected using western blot with a polyclonal antibody to HA (Fig. 2). The heterozygous SMCRT mice develop abnormalities at an adult stage (about 4-10 months old). The older mice become lethargic and inactive. Most of the male heterozygous animals develop skin lesions (Fig. 3) and hemangioma which can be detected on the skin. These mice suffer from lung congestion (Fig. 4) and kidney thrombosis (Fig. 5), symptoms resembling congestive heart failure. The evidence of heart failure is also observed in older (10-12 months) female heterozygous mice. Analysis of the kidney of the SMCRT mice showed hemorrhage from renal vessels in the renal adipose tissue and the presence of thrombus inside the kidney capsules (Fig. 5A, C). Histological analysis of the kidneys from the mice at end stage disease showed necrosis in

the kidney medulla and cortex (Fig. 6B, C). There was also increased blood accumulation in the kidney glomeruli (Fig. 7B) of the SMCRT mice as compared to the wild type glomeruli (Figure 7A). This could result in thrombosis in glomeruli. Histological analysis (Hematoxylin/Eosin) of the lungs of these mice we have seen congestion of the lungs and accumulation of blood in the alveoli (Fig. 4).